

## REMARKS

Claims 14-24, 34-43, and 49-69 are pending. Claims 14-16, 34, and 49 have been amended herein. Support for these amendments can be found throughout the specification and originally filed claims. No new matter has been added.

### *Rejection under 35 U.S.C. §112, first paragraph*

Claims 14-24, 34-43, and 49-69 were rejected under 35 U.S.C. §112, first paragraph as not enabled. The Examiner states that the as-filed application does not enable one skilled in the art to practice the invention without an undue amount of experimentation. In applying this rejection, the Examiner has focused upon three of the factors summarized by *In re Wands*, 858 F.2d 731 (1988), the scope of the claims, the unpredictability of the art, and the amount of experimentation required to enable one skilled in the art to practice the claimed invention. (See, Office action, page 2.) Applicants disagree for the reasons listed below.

### The scope of the claims.

The Examiner has indicated that the breath of the claims is directed to a method for preventing, inhibiting or treating bacterial, yeast, fungal and/or viral infections including vaginal infections by applying topically to skin or mucous membrane probiotic compositions with *Bacillus* species. (See, Office action at page 3.) The Examiner also states that the specification does not adequately teach how to inhibit bacterial, yeast, fungal and/or viral infections including vaginal infections because no animal cells or live animals were used, and that the burden for enabling the prevention of disease would be greater than of enabling treatment. (See, Office action at pages 3-4.) Applicants note that independent claim 14 has been amended herein to remove language directed to prevention, and to specify a method of inhibiting bacterial, yeast, fungal or viral infection by applying topically to skin or a mucous membrane of a mammal a probiotic composition comprising a bacterial component consisting of *Bacillus coagulans* bacteria. Further, amended claim 14 specifies that the *Bacillus coagulans* bacteria grow topically for sufficient time to inhibit growth of bacteria, yeast, fungus or virus. Similarly, claim 49 has been amended herein to replace the phrase, “preventing or treating a vaginal infection” with the phrase, “treating a vaginal infection.” The as-filed specification discloses the use of *Bacillus coagulans* bacteria to inhibit the growth of a representative number of pathogens. (See, e.g.,

Example 1, pages 24-27.) Therefore, Applicants assert that the inhibitory effectiveness of the *Bacillus coagulans* bacteria has been demonstrated without the use of *in vivo* animal models.

The predictability of the art.

The Examiner has indicated that the claims methods are drawn to a generic *Bacillus*, which would include pathogenic *Bacillus* species that would inhibit, if not kill, animal cells and animal models. Applicants note that the pending claims have been limited to probiotic *Bacillus coagulans* bacteria, which the specification discloses to have probiotic, antimicrobial activity. (See, e.g., page 12, line 19 to page 14, line 19.)

The Examiner has also stated that at least some strains of *Bacillus coagulans* do not inhibit all clinical *Staphylococcus* infections, citing Sytnik (Mikrobiologicheskii Zhurnal, 1989, 51:82-87). In response, Applicants assert that the specification discloses a number of exemplary probiotic *Bacillus coagulans* bacterial strains. (See, e.g., page 11, line 18 to page 12, line 10.) Moreover, the as-filed specification provides the means for one of ordinary skill in the art to determine the effectiveness of a given *Bacillus coagulans* bacterial strain in inhibiting a specific pathogen, including fungal, yeast, and bacterial pathogens. (See, e.g., page 24, line 1, to page 27, line 9.) One of ordinary skill in the art would be able to select a specific probiotic strain of *Bacillus coagulans* bacteria without undue experimentation.

The Examiner has also indicated that the art provides no reasonable expectation of success for claims drawn to inhibiting various topical and mucous membrane infections including vaginal infection, citing a passage in Seligman (British J. of Obstetrics and Gynaecology, 1995, 102:763-64) stating that studies in the use of *Lactobacilli* in the treatment of vaginitis and vaginosis have almost all been limited, uncontrolled, and have given variable results. (Seligman at page 763, paragraph 4.) However, in the next paragraph this reference describes a successful use of *L. acidophilus* in the control of candidal vaginitis by Hilton *et al.* (Annals Int. Med. 116:353-57, 1992). Thus, contrary to the Examiner's assertion, the state of the art provides a reasonable expectation of success.

The Examiner then states that Seligman also teaches that the ability of bacteria to adhere to animal epithelial cells is an important factor in colonization of mucous membrane or vagina and that different species show varying effects. (See, Office action, page 5.) In this case, Applicants have amended the claims to require a particular species of *Bacillus*, i.e., *Bacillus*

*coagulans*. Moreover, the specification discloses that *Bacillus coagulans* strains can colonize tissue, including skin and mucous membrane tissues. (See, *e.g.*, page 7, lines 6-19.) Applicants have addressed this issue by amending the claims to require a species of *Bacillus coagulans*, that adheres to and colonizes skin and mucous membrane tissues.

The amount of experimentation required.

The Examiner states that the claimed doses and or protocols for administration are generic considerations and they have not been demonstrated in models involving animal cells and/or live animals and because the claimed doses have not been demonstrated to be effective for colonization of the skin or mucous membrane, including vagina. (Office action at page 6.) The Examiner also states that the specification does not teach how to extrapolate data obtained from *in vitro* biological studies to the development of *in vivo* mammalian (*e.g.*, human) treatment. (Id.) Applicants disagree. The as-filed specification discloses the use of specific concentration of *Bacillus coagulans* bacteria to inhibit the growth of a representative number of pathogens as compared to a positive control treatment of 2% miconazole provided in a similar volume. (See, *e.g.*, Example 1, pages 24-27.) Not only is one skilled in the art able to use the relative amounts of the *Bacillus coagulans* bacterial composition and the positive control miconazole to extrapolate specific effective dosages for *in vivo* treatment of humans and other mammals, the specification in numerous places (*e.g.*, page 27, lines 16, 23 and 30; page 28, line 8; page 30, line 9 to page 31, line 5; page 31, line 12 to page 32, line 3; page 32, lines 4-14; page 32, line 23 to page 33, line 2; page 33, lines 15-22; page 34, lines 6-12; page 35, lines 21-27; page 36, lines 8-11 and 15-18; and page 37, lines 8-9) provides specific ranges or absolute amounts of bacteria or spores to be used in the claimed methods. For this reason, an ordinary practitioner would be able to use the claimed methods without undue experimentation.

For the above-stated reasons, Applicants assert that the methods as presently claimed are predictable and that the level of experimentation left to the skilled practitioner is not unnecessary, improper, extensive, or undue. Therefore, the pending claims, as amended herein, are fully enabled, and this rejection should be withdrawn.

### ***Rejection under 35 U.S.C. §102***

Claims 14-16, 24, 34-39, 49-50, 55-57, and 65-67 were rejected under 35 U.S.C. §102(b) as anticipated by Hata *et al.* (U.S. patent number 4,871,539). The Examiner states that Hata discloses a method of using a probiotic composition with *Bacillus* species including *Bacillus coagulans* topically to pubic and vaginal areas. (See Office Action at page 7).

In response, Applicants note that pending independent claims 14, 34 and 49 have been amended herein to specify a composition comprising a bacterial component consisting of *Bacillus coagulans* bacteria. Thus, claims 14, 34 and 49, as currently amended, exclude other bacterial strains. Hata only teaches the use of *Bacillus coagulans* in combination with other bacteria-- specifically *Lactobacillus clearans* and optionally *Streptococcus faecalis*. (See, Hata, Table 4.) Therefore, Hata does not teach all the limitations of claims 14, 34 and 39. Thus, these claims are not anticipated by Hata. Claims 15-16, 35-39, 50, 55-57 and 65-67 depend, directly or indirectly, on claims 14, 34, or 49 and, therefore, contain all the limitations of the independent claims. Thus, these claims are also not anticipated by Hata.

For these reasons, Applicants therefore request withdrawal of this rejection.

### ***Rejection under 35 U.S.C. §103***

Claims 14-16, 20-22, 24, 34-39, 41-43, 49-50, 55-57, and 59-67 were rejected under 35 U.S.C. §103(a) as unpatentable over Hata in view of Gibson *et al.* (Gastroenterology (1995) 109:975) and Japanese patent application JP 3-192200. The Examiner states that Hata does not disclose the use of sugars such as FOS and additional bath oils, salts, and surfactants, but that Gibson teaches that the addition of FOS stimulates probiotic bacteria that contact a mucous membrane, and that JP 3-192200 teaches the addition of salts and surfactants into detergent compositions with *Bacillus coagulans*. (See Office Action at pages 8-9). As discussed above, Hata only teaches the use of *Bacillus coagulans* in combination with other bacteria (*Lactobacillus clearans* and, optionally, *Streptococcus faecalis*), but pending claims 14-16, 20-22, 24, 34-39, 41-43, 49-50, 55-57, and 59-67, as currently amended, exclude other bacterial strains. Therefore, Hata lacks a limitation of these claims. Gibson and JP 3-192200 do not cure this deficiency, as neither reference teach methods of topically applying a probiotic composition containing only *Bacillus coagulans* bacteria. Thus, pending claims 14-16, 20-22, 24, 34-39, 41-

43, 49-50, 55-57, and 59-67 are not obvious in view of the combination of Hata, Gibson, and JP 3-192200. This rejection should be withdrawn.

## CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that this paper is fully responsive and that the pending claims are in condition for allowance. Such action is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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